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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/008,355	11/08/2001	James Travis	235.00440101	4382

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EXAMINER

SWOPE, SHERIDAN

ART UNIT	PAPER NUMBER
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1652

DATE MAILED: 07/13/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

10/008,355

Applicant(s)

TRAVIS ET AL.

Examiner

Sheridan L. Swope

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 30 September 2002.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 10-18 and 24-38 is/are pending in the application.
- 4a) Of the above claim(s) 14-18 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 10-13 and 24-38 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☒ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.
- If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

- 13) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.
- 14) ☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
- a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☒ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) 9&10.
- 4) ☐ Interview Summary (PTO-413) Paper No(s). _____.
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other: _____.

DETAILED ACTION

Applicant's election with traverse of Invention II, Claims 10-13 in Paper No. 7 is acknowledged. The traversal is on the ground(s) that no undue burden would be imposed by examination of multiple groups, such as I-VI, since searches for these groups would overlap significantly. This is not found persuasive Groups I-V are distinct for the reasons described in the prior action. For Groups I-V, a search for one group would not encompass a search for any other group and searching all groups would represent a burden on the Office. Rejoinder of inventions will be considered if this application should be found allowable. The restriction requirement is still deemed proper and is therefore made FINAL.

Applicant's cancellation of Claims 1-9 and 19-23 as well as addition of Claims 24-38 in Paper No 8 is acknowledged. Claims 14-18 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to non-elected Inventions, there being no allowable generic or linking claim. New Claims 24-38 recite dipeptidylpeptidase DNA molecules and hence, will be incorporated into Invention II. Claims 10-13 and 24-38 are hereby examined on their merits.

Claim Rejections - 35 USC § 112-Second Paragraph

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 10-12 and 24-38 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Claims 10, 24, and 35 recite isolated nucleic acid molecules that encode dipeptidylpeptidases "...having amidolytic activity...wherein, the target polypeptide has an aliphatic or an aromatic residue...". The term "aliphatic or aromatic residue" is

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indefinite, as specific amino acids are not recited. Is glycine considered to be aliphatic? Is tyrosine considered to be polar or aromatic? Lack of clarity on the answers to these two questions causes Claims 10, 24, and 35 to be indefinite in reciting “aliphatic or aromatic residue”. Since Claims 11 and 12 are dependent on Claim 1, Claims 25-34 are dependent on Claim 35, and Claims 36-38 are dependent on Claim 35, all said claims are rejected under 35 U.S.C. 112, second paragraph for the reasons above.

Claim 12 is further rejected under 35 U.S.C. 112, second paragraph, as being indefinite. The phrase “...three for 20 minutes washes...” is worded poorly; it should be “...three washes of 20 minutes each...”. Also, it is not clear whether the nucleic acid recited hybridizes to the full-length of SEQ ID NO: 1 or to a 20-nucleotide fragment of SEQ ID NO: 1. Clarification is required. For purposes of examination, it is assumed that the nucleic acid of Claim 12 may hybridize to as little as 20 nucleotides of SEQ ID NO: 1.

Claims 29-34 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Claims 29-34 are totally unclear in the recitation of “...in register with residues 644-653 of SEQ ID NO: 2”.

Claim Rejections - 35 USC § 112-First Paragraph

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

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Claims 10, 12, 13, and 24-31 are rejected under 35 U.S.C. 112, first paragraph. The specification is enabling for the dipeptidylpeptidase encoded by SEQ ID NO: 1 and set forth by SEQ ID NO: 2. However, the specification does not reasonably provide enablement for any nucleic acid molecule encoding any dipeptidylpeptidase activity having amidolytic activity. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims.

Claim 10 is so broad as to encompass any nucleic acid molecule encoding any dipeptidylpeptidase activity having amidolytic activity. Claim 12 is so broad as to encompass any nucleic acid molecule encoding any dipeptidylpeptidase activity having amidolytic activity wherein the complement of said molecule hybridizes under conditions of 0.5M phosphate buffer, pH 7.2, 7% SDS, 10mM EDTA, at 68C, followed by three for 20 minutes washes in 2X SSC, and 0.1% SDS, at 65C, wherein at least about 20 nucleotides of the complement hybridizes. Claim 13 is so broad as to encompass encompass any nucleic acid molecule encoding any dipeptidylpeptidase activity wherein the encoded polypeptide has a sequence that is greater than about 40% identity with SEQ ID NO: 2. Claim 24 is so broad as to encompass any nucleic acid molecule encoding any dipeptidylpeptidase activity having amidolytic activity and comprising the sequence TGGNSGSPV (SEQ ID NO: 26). Claim 25 is so broad as to encompass any nucleic acid molecule encoding any dipeptidylpeptidase activity having amidolytic activity and comprising the sequence TGGNSGSPVF (SEQ ID NO: 25). Claim 26 is so broad as to encompass any nucleic acid molecule encoding any dipeptidylpeptidase activity having amidolytic activity and comprising residues 543-712 of SEQ ID NO: 2. Claim 27 is so broad as

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to encompass any nucleic acid molecule encoding any dipeptidylpeptidase activity having amidolytic activity and comprising residues 540-712 of SEQ ID NO: 2. Claim 28 is so broad as to encompass any nucleic acid molecule encoding any dipeptidylpeptidase activity having amidolytic activity and comprising residues 522-712 of SEQ ID NO: 2. Claims 29-31 are so broad as to encompass any nucleic acid molecule encoding any dipeptidylpeptidase activity having amidolytic activity wherein, the encoded polypeptide has greater than 40%, 50%, or 60%, respectively, identity with SEQ ID NO: 2 and comprises the sequence TGGNSGSPVF (SEQ ID NO: 25) in register with residues 644-653 of SEQ ID NO: 2. The scope of each of these claims is not commensurate with the enablement provided by the disclosure with regard to the extremely large number of polynucleotides broadly encompassed by the claim. Since the amino acid sequence of a protein determines its structural and functional properties, predictability of which changes can be tolerated in a protein's amino acid sequence and obtain the desired dipeptidylpeptidase activity requires a knowledge of and guidance with regard to which amino acids in the protein's sequence, if any, are tolerant of modification and which are conserved (i.e. expectedly intolerant to modification), and detailed knowledge of the ways in which the protein's structure relates to its function. However, in this case the disclosure is limited to the amino acid sequence of SEQ ID NO 2 and the nucleotide sequence of SEQ ID NO 1.

While recombinant and mutagenesis techniques are known, it is not routine in the art to screen for multiple substitutions or multiple modifications, as encompassed by the instant claims, and the positions within a protein's sequence where amino acid modifications can be made with a reasonable expectation of success in obtaining the desired activity/utility are limited in any protein and the results of such modifications are unpredictable. In addition, one skilled in the art

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would expect any tolerance to modification for a given protein to diminish with each further and additional modification, e.g. multiple substitutions.

The specification does not support the broad scope of (i) Claim 10 encompassing any nucleic acid molecule encoding any dipeptidylpeptidase activity having amidolytic activity; (ii) Claim 12 encompassing any nucleic acid molecule encoding any dipeptidylpeptidase activity having amidolytic activity wherein the complement of said molecule hybridizes under conditions of 0.5M phosphate buffer, pH 7.2, 7% SDS, 10mM EDTA, at 68C, followed by three for 20 minutes washes in 2X SSC, and 0.1% SDS, at 65C, wherein at least about 20 nucleotides of the complement hybridizes; (iii) Claim 13 encompassing any nucleic acid molecule encoding any dipeptidylpeptidase activity wherein the encoded polypeptide has a sequence that is greater than about 40% identity with SEQ ID NO: 2; (iv) Claim 24 encompassing any nucleic acid molecule encoding any dipeptidylpeptidase activity having amidolytic activity and comprising the sequence TGGNSGSPV (SEQ ID NO: 26); (v) Claim 25 encompassing any nucleic acid molecule encoding any dipeptidylpeptidase activity having amidolytic activity and comprising the sequence TGGNSGSPVF (SEQ ID NO: 25); (vi) Claim 26 encompassing any nucleic acid molecule encoding any dipeptidylpeptidase activity having amidolytic activity and comprising residues 543-712 of SEQ ID NO: 2; (vii) Claim 27 encompassing any nucleic acid molecule encoding any dipeptidylpeptidase activity having amidolytic activity and comprising residues 540-712 of SEQ ID NO: 2; (viii) Claim 28 encompassing any nucleic acid molecule encoding any dipeptidylpeptidase activity having amidolytic activity and comprising residues 522-712 of SEQ ID NO: 2; (ix) Claims 29-31 encompassing any nucleic acid molecule encoding any dipeptidylpeptidase activity having amidolytic activity wherein, the encoded polypeptide has

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greater than 40%, 50%, or 60%, respectively, identity with SEQ ID NO: 2 and comprises the sequence TGGNSGSPVF (SEQ ID NO: 25) in register with residues 644-653 of SEQ ID NO: 2.

The specification does not support the broad scope of Claims 10, 12, 13, and 24-31 because the specification does not establish: (A) regions of the protein's structure which may be modified without effecting the dipeptidylpeptidase activity; (B) the general tolerance of the dipeptidylpeptidase activity to modification and extent of such tolerance; (C) a rational and predictable scheme for modifying any residues with an expectation of obtaining the desired biological function; and (D) the specification provides insufficient guidance as to which of the essentially infinite possible choices is likely to be successful.

Thus, applicants have not provided sufficient guidance to enable one of ordinary skill in the art to make and use the claimed invention in a manner reasonably correlated with the scope of the claims broadly including any number of nucleic acid molecules encoding proteins with dipeptidylpeptidase activity having an enormous number of amino acid modifications of the dipeptidylpeptidase of SEQ ID NO: 2. The scope of the claims must bear a reasonable correlation with the scope of enablement (*In re Fisher*, 166 USPQ 19 24 (CCPA 1970)). Without sufficient guidance, determination of the identity of sequences having the desired biological characteristics is unpredictable and the experimentation left to those skilled in the art is unnecessarily, and improperly, extensive and undue. See *In re Wands* 858 F.2d 731, 8 USPQ2d 1400 (Fed. Cir, 1988).

Claims 10, 12, 13, and 24-28 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to

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reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

These claims are directed to a genus of DNA molecules encoding any dipeptidylpeptidase activity from any source. The specification teaches the structure of only a single representative species of such DNAs. Moreover, the specification fails to describe any other representative species by any identifying characteristics or properties other than the functionality of encoding a dipeptidylpeptidase activity. Given this lack of description of representative species encompassed by the genus of the claim, the specification fails to sufficiently describe the claimed invention in such full, clear, concise, and exact terms that a skilled artisan would recognize that applicants were in possession of the claimed invention.

Claim 13 is rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This claim is directed to a genus of DNA molecules encoding any polypeptide with greater than about 40% identity with either SEQ ID NO:2.

The specification does not contain any disclosure of the function of all DNA molecules encoding any polypeptide with greater than about 40% identity with either SEQ ID NO:2. The genus of cDNAs that comprise these above cDNA molecules is a large variable genus with the potentiality of encoding many different proteins. Therefore, many functionally unrelated DNAs are encompassed within the scope of this claim, including partial DNA sequences. The specification discloses only a single species of the claimed genus which, is insufficient to put one of skill in the art in possession of the attributes and features of all species within the claimed

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genus. Therefore, one skilled in the art cannot reasonably conclude that the applicant had possession of the claimed invention at the time the instant application was filed.

Applicant is referred to the revised guidelines concerning compliance with the written description requirement of U.S.C. 112, first paragraph, published in the Official Gazette and also available at www.uspto.gov.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 10-13 and 13 and 24-38 are rejected under 35 U.S.C. 102(a) or (b) over applicant's admission of the prior art. As disclosed by the specification (Example 6), the data-base TIGR was used to obtain the full-length sequence for DPP-7, as presented in Fig 4 and set forth by SEQ ID NO: 2. TIGR is a publicly available data base from The Institute for Genomic Research (see enclosed TIGR The Institute for Genomic Research; Frequently Asked Questions, question 10). As described in the specification (page 26, line 16), applicants obtained the sequence set forth by SEQ ID NO: 2 from TIGR wherein said sequence designated P. Gingivalis genomic contig gln / TIGR / P.gingivalis_1208. Therefore, Claims 10-13 and 24-38 are rejected under 35 U.S.C. 102(a) or (b) over applicant's admission of the prior art. It is requested that applicant's submit any documentation disclosing their discovery that SEQ ID NO: 2 was available from the TIGR data base and/or when the sequence P. Gingivalis genomic contig gln / TIGR / P.gingivalis_1208 was available to the public via the TIGR data base.

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Claim 24 is rejected under 35 U.S.C. 102(b) as being anticipated by Simpson et al, 2000. Simpson et al teach a polynucleotide comprising a sequence at nucleotide residues 8535-8561 which encodes SEQ ID NO: 26 and is a peptidase (specification page 31, lines 22-24). The Office does not have the facilities to determine whether the sequence taught by Simpson et al has dipeptidylpeptidase activity. The burden is on the applicant to prove that the polynucleotide taught by Simpson et al does not disclose the invention of Claim 24. Therefore, Claim 24 is rejected under 35 U.S.C. 102(b) as being anticipated by Simpson et al, 2000.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Sheridan L. Swope whose telephone number is 703-305-1696. The examiner can normally be reached on M-F; 9:30-7 EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ponnathapura Achutamurthy can be reached on 703-308-3804. The fax phone numbers for the organization where this application or proceeding is assigned are 703-305-3014 for regular communications and 703-872-9307 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.

Sheridan L. Swope, Ph.D.


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